In regard to application # 08/986,606;
12/08/97 #5

Dear Avis M. Davenport, Primary examiner
Group 1654:

I am writing to rebut the criticism that resulted in your rejection of my claims:

1. The time frames for the patent application relative to previous patents and patent applications are as follows:

a. U.S. Patent 5,298,604, Mar 29 '94 deals with the protein N-terminal amino acid sequence

b. Ridge and Sloane, cytokine Jan 1996 - nonapeptide - N-terminal sequence of ANUP possesses 10% of anti-tumor activity of the cytokine

c. Sloane - U.S. patent application on pharmacologically active anti-tumor activity of the nonapeptide activated by SDS. application 08/641,905 filed May 2, 1996. this application is now being reviewed; see

Sloane 08/486,606 12/8/97 2.

enclosed letter and ? = enclosed
reprint Sloane and Davis Jan 1996
Tumor Targeting (1996) 2, 322-326
the Sloane patent application of
12/08/97 #08/486,606 deals with the
pharmacologically anti tumor activity
of the 16 amino acid N-terminal
peptide.

This data has not been published

the 50% activity of the 16 amino
acid peptide is a great advance
over the 10% activity of the
nonapeptide

Prior art can not anticipate the
very large increase in pharmacologically
anti tumor activity of the 16 amino
acid peptide over that of the 9 amino
acid peptide. It is possible that
there could be no increase in
activity - thus the one year prior
date does not apply

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P.S.

The determination of the N-terminal Amino acid sequence was thoroughly described in publication Ridgeand Sloane, Cytokine (1996) 8, pp. 1-5 and documented in U.S. Patent #5,298,604 date Mar 29, 1994

The synthesis of amino acid sequences are routinely performed and is well known throughout the scientific community, there are many chemical companies that employ the experties to provide synthetic peptides world wide. We have used one such company, Research Genetics of Huntsville, Alabama.

The use of the 16 Amino acid peptide is well delineated in claim 1. "The use of the 16-

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representing the partial N-terminal amino sequence of the antineoplastic protein (ANUP) as a pharmacologically anti-tumor agent which kills only human tumor cells (using the human breast tumor cell line as a model)"

We certainly can delete the parentheses

We had previously determined that a very diverse number of human tumor cells were killed by the cytokine (ANUP) in vitro and in vivo.

see a) Sloane et al Biochemical J. (1986) 234; pp355-362, and

Sloane and Davis (1996) Tumor Targeting 2, 322-326.

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We previously determined that a diverse number of human tumor cell lines were specifically killed by ANUP which included, breast, lung, bladder, cervix, melanoma, and pancreas. Indeed Sloane and Davis (Tumor Targeting (1996) 2 322-326. showed that the protein was active in vivo as a pharmacologically active anti-tumor protein - the protein ANUP caused the regression of both cervical tumor cells and laryngeal tumor cells (each of human origin) when injected in nude mice.

Since the 16 amino N-terminal epitope of ANUP represents the active anti-tumor portion of ANUP

than the use of the peptide by parenteral injection as used in studies with the protein would be indicated. Indeed U.S. Patent issued on the antineoplastic protein (ANUP) - U.S. Patent #5,298,604 issued Mar 29, 1994 has recorded such a use see patent column 4 under "Biological Properties of ANUP"

"this antitumor chemotherapeutic agent to treat human neoplastic disease. The view of potential use of ANUP in Cancer therapy is justified by the following

a ANUP is non-toxic to human cells;
b ANUP specifically inhibits only human cancer cell lines
c ANUP causes regression

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of human tumor cell lines
implanted in nude mice."

thus claims 1 and 3 for the use of
the 16 K-amino acid peptide does
indeed set forth steps in the use of
the peptide as an anti-tumor agent
by parenteral injections as shown
in the U.S. patent of Sloane
#5,298,604 date Mar 29, 1994
and publications of Sloane
and Davis, Tumor Targeting
(1996) 2, 322-326.

thus the potential use of
the 1-16 amino acid peptide is
clearly indicated as shown by
above references and clear
demonstration of the effect

of ANUP in causing the regression of human tumor cells implanted in nude mice upon parenteral injection.

Claim 3 relates to the activation of the 16 amino acid peptide as clearly delineated in the "Description of the Preferred Embodiment."

Also similar to the present application, equivalent activity was noted between the new Compound and the naturally-occurring Compounds. In his opinion Judge Rich states:

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1) where no particular utility is recited for a compound, evidence of any utility is adequate (citing Blicke v Treves 112 USPQ 472);

2) "tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use"

3) "[S]ince it is crucial to provide researchers with an incentive to disclose pharmacological activity in as many compounds as possible, we conclude that adequate proof of any such activity constitutes

a showing of practical utility" and

4) "the controlling point is ..... evidence of pharmacological activity."

If I am unclear at any point please call me at

901-754-7848

Sincerely

Nathan Sloane